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10/666,998	09/19/2003	Andrei Laikhter	013670-9004 US00	1003

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EXAMINER

STAPLES, MARK

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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01/08/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/666,998

Applicant(s)

LAIKHTER ET AL.

Examiner

Mark Staples

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10/15/2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 37-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 37-50 is/are rejected.
- 7) ☒ Claim(s) 50 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 19 September 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

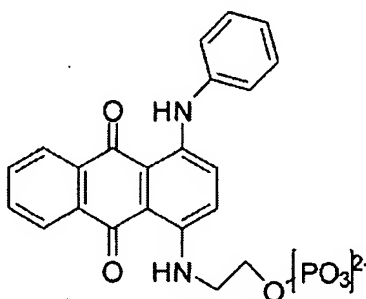
- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____  |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :10/31/03, 02/17/04, 10/26/04, 06/20/05, 10/10/06, & 09/14/07.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of claims 30-34 of Group II and the specie election of the anthraquinone quencher shown:



and the cancellation of claims 1-36 and the submission of new claims 37-50 in the reply filed on 10/15/2007 is acknowledged.

Claims 37-50 are pending and at issue.

Election was made **without** traverse in the reply filed on 10/15/2007.

### *Specification*

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should reflect that the pending claims are only directed to method of use and not to methods of preparation.

3. The use of the trademarks TEXAS RED™ and CY5™ have been noted in this application. They and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to scan the entire application to ensure trademark usage in all the places where it appears in the application is in compliance with the current office guidelines.

### ***Drawings***

4. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the axes of Figure 2 are illegible. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
7. The use of the terms "comprise" or "comprises" for variables such as R1-R14 and Z renders the claims indefinite because it is not clear what else can be included in these groups.
8. The recitation of "Z comprises a linking group or bond" renders the claim more indefinite as it is not clear what can be a "linking group" and it is unclear as to what the "bond" can be but how another bond can be included as Z in formula 2 without at least one other atom as Z. Such an atom or atoms substituting for Z is/are also undefined and hence unclear.
9. The recitation of "electron pair" and "linker" render the claim indefinite as these are not defined, and hence unclear, as to what atom(s) necessarily accompany the "electron pair" and what the composition of the linker is.

***Formulas I and II of Claim 50 are Unsearchable***

10. A preliminary examination of this application reveals that it includes terminology which is so different from that which is generally accepted in the art to which this invention pertains that a proper search of the prior art cannot be made. For example: formulas I and II of claim 50 are unsearchable as the structures of these formulas are indefinite. See rejections above under 35 U.S.C. 112, second paragraph.

Applicant is required to provide a clarification of these matters or correlation with art-accepted terminology so that a proper comparison with the prior art can be made. Applicant should be careful not to introduce any new matter into the disclosure (i.e., matter which is not supported by the disclosure as originally filed).

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Batz et al. (United States Patent No. 6,117,973 issued September 12, 2000).

Regarding claim 37, Batz et al. teach a method of detecting fluorescence of a fluorophore in a system comprising the fluorophore and a nucleic acid polymer comprising an anthraquinone quencher attached thereto, comprising detecting the fluorescence of the system (see column 21 lines 42-63).

Regarding claim 38, Batz et al. teach wherein a change in fluorescence of the system is correlated with a change in the spatial relationship between the quencher and the fluorophore (see column 21 lines 42-63 and column 22 lines 1-20).

Regarding claim 39, Batz et al. teach wherein the fluorophore is attached to the nucleic acid polymer comprising the anthraquinone quencher (in a PBA hairpin system, see column 21 lines 42-63).

Regarding claim 40, Batz et al. teach wherein the fluorophore and anthraquinone quencher are attached to the polymer such that the fluorescence of the fluorophore is reduced (see column 22 lines 1-20).

Regarding claim 41, Batz et al. teach wherein the nucleic acid polymer forms a random-coil conformation when the nucleic acid polymer is unhybridized, such that the fluorescence of the fluorophore is reduced (see column 21 lines 42-63 and column 22 lines 1-20).

Regarding claim 42, Batz et al. teach wherein the system is a system for detecting a target nucleic acid having a sequence complimentary to at least a portion of the nucleic acid polymer, hybridization of the nucleic acid polymer to the target nucleic acid causing a change in fluorescence indicative of the presence of the target nucleic acid (see column 23 lines 9-27 and see Figure 6).

Regarding claim 43, Batz et al. teach wherein the nucleic acid polymer comprises a self- complimentary sequence and wherein the quencher and the fluorophore are attached to the nucleic acid polymer such that the fluorescence of the fluorophore is quenched by the anthraquinone quencher when the nucleic acid polymer undergoes intramolecular base pairing (see column 23 lines 9-50 and see Figure 6).



Regarding claim 44, Batz et al. teach wherein hybridization of the polymer to the target nucleic acid results in an increase in fluorescence of the fluorophore (see column 23 lines 9-50 and see Figure 6).

Regarding claim 45, Batz et al. teach wherein the fluorophore is attached to a second nucleic acid polymer, and wherein the first and second nucleic acid polymers hybridize to two adjacent regions of the target nucleic acid such that when both polymers hybridize to the target nucleic acid the fluorescence of the fluorophore is reduced (see Figure 3 and its description in column 22 lines 56-61).

Regarding claim 46, Batz et al. teach wherein the fluorophore is attached to a second nucleic acid polymer complimentary to the first nucleic acid polymer, such that when the first and second nucleic acid are hybridized, the fluorescence of the fluorophore is reduced (see column 23 lines 51-63 and Figure 7).

Regarding claim 47, Batz et al. teach wherein the system further comprises a target nucleic acid comprising a sequence that hybridizes to the first or second nucleic acid polymer, hybridization of the target nucleic acid to the first or second nucleic acid polymer causing an increase in fluorescence (see column 23 lines 51-63 and Figure 7).

Regarding claim 49, Batz et al. teach wherein the system is a PCR reaction, mixture wherein synthesis of product, which is an amplicon, results in a change in fluorescence (see column 23 line 22-27).

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Batz et al. as applied to claim 37 above, and further in view of Jenne et al. (United States Patent No. 6,451,535 issued September 17, 2002).

Batz et al. teach as noted above.

Batz et al. do not specifically teach separation of an anthraquinone quencher from a fluorophore by cleaving an RNase restriction site between them.

Regarding claims 48, Jenne et al. teach wherein the system is a system for measuring RNase activity, wherein the nucleic acid polymer is a ribonucleic acid polymer comprising the fluorophore attached thereto, wherein the ribonucleic acid polymer comprises an RNase restriction site between the quencher and the fluorophore, a change in fluorescence indicating the presence of RNase which is ribonuclease P (see Figure 1 and see column 2 lines 32-40).

Jenne et al. do not teach an anthraquinone quencher.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Jenne et al. by substituting an anthraquinone quencher as suggested by Batz et al. with a reasonable expectation of success. The motivation to do so is provided by Batz et al. who teach that anthraquinones are preferred acceptors/quenchers (see column 15 line 44) in quencher and fluorophore pairs and the teaching of Jenne et al. that that quencher and fluorophore pairs can be used to monitor RNase activity (entire patent, especially Figure 1 and see column 2 lines 32-40). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

#### ***Allowable Subject Matter***

15. Claim 50 would be allowable for the elected species if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

16. The following is a statement of reasons for the indication of allowable subject matter: no prior art was found which teaches or fairly suggests the elected species of the compound shown above. A structure search for the compound was conducted and no prior was found which taught or fairly suggested this compound.

***Conclusion***

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

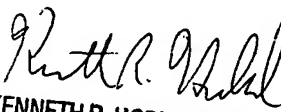
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Mark Staples  
Examiner  
Art Unit 1637  
January 7, 2008

MS

  
KENNETH R. HORLICK, PH.D  
PRIMARY EXAMINER

1/7/08